510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number: K032332

B. Analyte: quinidine

C. Type of Test: homogeneous microparticle immunoassay

D. Applicant: Roche Diagnostics Corporation

E. Proprietary and Established Names: Roche Online TDM Quinidine Assay

F. Regulatory Information:

1. Regulation section:
   21 CFR 862.3320, Quinidine Test Systems have been regulated under 21 CFR 862.3320, Digoxin Test System.
2. Classification:
   Class II
3. Product Code:
   91 LBZ
4. Panel:
   Toxicology

G. Intended Use:

1. Indication(s) for use:
   The Roche ONLINE TDM Quinidine assay is for the quantitative determination of quinidine in human serum or plasma on automated clinical analyzers. Quinidne is used for the prevention and treatment of ventricular arrhythmias, junctional (nodal) arrhythmias and supraventricular (atrial) arrhythmias. The quinidine dosage required to achieve therapeutic serum levels is dependent on the drug formulation, patient age and individual variability in absorption and metabolism. The proposed labeling indicates the Roche/Hitachi 911, 912, 917 and Modular P analyzers can be used with the Roche ONLINE Quinidine reagent kits.
2. Special condition for use statement(s):
   For prescription use.
3. Special instrument Requirements:
   The test is for use on automated clinical chemistry analyzers including the Roche Hitachi 911, 912, 917 and Modular P.

H. Device Description:

The test consists of ready-to-use reagents including anti-quinidine monoclonal antibody and conjugated quinidine-derivative microparticles with buffers and preservatives.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche Cobas Integra Quinidine

2. Predicate K number(s):
   K951595

3. Comparison with predicate:
   The devices are similar in terms of intended use and indications for use. They each use different technologies. Detection of the analyte in the predicate assay is based on fluorescence polarization. Detection in this assay is based on changes in scattered light resulting from microparticle aggregation.

J. Standard/Guidance Document Referenced (if applicable):

K. Test Principle:

The test is a homogenous assay based on measuring changes in scattered light resulting from aggregation of microparticles. Microparticles coated with quinidine aggregate in the presence of the quinidine antibody. Samples containing quinidine inhibit the aggregation to varying degrees depending on the quinidine concentration.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. *Precision/Reproducibility:*
   Precision was evaluated on the Hitachi 917 at the manufacturer's site using control material and spiked human serum pools. The evaluation included 3 runs/day over 21 days. Calculations were similar to those described in NCCLS EP-5A. Recalibrations were performed several times during the evaluation as necessary for changes in reagent. Results are tabulated below:

Specimen	Low spike	High spike	Control 1	Control 2	Control 3
Total mean (ug/ml)	2.04	6.32	0.93	2.87	4.6
Within-run SD (ug/ml)	0.020	0.088	0.018	0.036	0.057
Within-run %cv	1.0	1.4	2.0	1.3	1.2
Total SD (ug/ml)	0.050	0.218	0.034	0.074	0.122
Total %CV	2.5	3.4	3.7	2.6	2.6
Between-day SD (ug/ml)	0.046	0.199	0.029	0.065	0.107
Between-day %CV	2.3	3.1	3.1	2.3	2.3

b. Linearity/assay reportable range:

The reportable range, based on the upper limit of the linear range and the limit of the blank (sensitivity), is 0.09-8.0 ug/ml. To evaluate linearity, spiked human serum pools were diluted with a quinidine negative human serum pool in a dilution series. Percent recoveries across the range are tabulated below. Values shown represent the median of triplicate measurements. Percent recoveries ranged from 101-92%, trending downward at higher quinidine concentrations.

Measured value	Theoretical value	% recovery (measured/theoretical)
0.05	-0.04	
1.160	1.175	98.7
2.410	2.389	100.9
3.640	3.603	101.0
4.790	4.816	99.5
6.030	6.030	100.0
6.790	7.244	93.7
7.780	8.457	92.0
8.810	9.671	91.1

c. Traceability (controls, calibrators, or method):

Controls and calibrators were previously cleared (K951595 and K981532) and are sold separately.

d. Detection limit:

The detection limit of 0.09 ug/ml is based on the mean and two standard deviations of 21 determinations of zero calibrator material. A linear interpolation model, based on these determinations of the zero calibrator material, as well as five replicate determinations of the 0.5 calibrator material, was used to calculate the concentration equivalent to the mean plus two standard deviations.

e. Analytical specificity:

To evaluate potential interference from drugs and metabolites, serum pools were spiked with drugs or metabolites and 5 ug/ml quinidine. Any drug found to cross-react at high concentrations was run in a series of dilutions. Percent cross reactivity for drugs and metabolites were defined as:

[(Da-Dt)/C]x100, where Dt = the measured concentration of the control analyte, Da = measured concentration of the control analyte + cross-reactant and C= known concentration of cross-reactant. Calculated cross-reactivities are based on the median of triplicate determinations. Observed cross-reactivities with the compounds tested are tabulated below:

Compound	Concentration (ug/ml)	% cross-reactivity
Dihydroquinidine	1	53
O-desmethylquinidine	10	18.1
Quinine	20	11.3
2'-oxoquinidone	50	5.3
10,11-dihydroquinidinediol	50	4.1
Hydrochlorothiazide	4.5	3.8
Isoproterenol	5	3.0
Quinidine-N-oxide	100	2.3
Disopyramide	80	0.9
Lidocaine-N-ethylbromide	50	0.5
Phenytoin (DPH)	200	0.2
N-Acetylprocainamide	200	0.1
3(S)-Hydroxyquinidine	100	0.1

No cross-reactivity was detected for the following drugs (concentrations in ug/ml): digitoxin (0.4), digoxin (0.022), ephedrine (1.2), Furosemide (100), ouabain (0.002), procainamide (80), propranolol (3.4), reserpine (0.1).
Sixteen common drugs were tested for interference. Recoveries of quinidine in this sample ranged from 96-109%. No significant interference was observed for the following drugs at the concentrations tested (concentrations in ug/ml): acetylcysteine (150) , ampicillin (1000) , ascorbic acid (300) , K-Dobesilate (200), methyldopa (20), Doxycycline (50), cyclosporine (5), levodopa (20), metronidazole (200), phenylbutazone (400) , acetylsalicylic acid (1000) , rifampicin (60), acetaminophen (200), ibuprofen (500), cefoxitin (2500), theophylline (100).

To evaluate interference from endogenous compounds, a series of dilutions containing varying levels of the endogenous compounds was prepared from spiked and negative serum pools. Testing was in the presence of 2 ug/ml quinidine (except for HAMA testing, in which samples contained 5 ug/ml quinidine.) Percent recovery was calculated relative to control samples containing quinidine without spiked endogenous compounds. The median of triplicate determinations was used in calculations of recovery. Concentrations ranges of endogenous compound in which assay recovery ≥ 90% is observed are tabulated below:

Compound/sample condition tested	Concentration range within recovery criteria (+/- 10% bias)	Recoveries/ trends observed
Bilirubin (conjugated and unconjugated)	I index up to 66 (approximately equivalent to 66 mg/dL)	Near 100% at low bilirubin concentrations, decreasing to 93% at values (of unconjugated bilirubin) between 65 and 70 mg/dL
Hemoglobin	I index up to 1000 (approximately equivalent to1000 mg/dL)	Near 100% at lower levels increasing to 107% at I index values near 1000
Lipemia	L index up to 2000 (approximately equivalent to 2000 mg/dL intralipid)	Recoveries range from 100-95%.
Rheumatoid factor	Up to 1200 IU/ml	Near 100% at low levels, decreasing to 90% at levels near 1200 IU/ml
Samples containing HAMA 1 and HAMA 2		95-100 % recovery
Total protein	Range: 0-11.8 g/dL	92-105% recovery. Lower recoveries observed at both ends of the range.

Clinical samples (n=7) containing triglycerides in the range 100-1700 mg/dL were tested. Recoveries ranged from 100- 83%, however, no clear trends were observed. (The sample with lowest recovery contained 800 mg/dL triglycerides).

f. *Assay cut-off:*
NA. This is a quantitative assay.

2. Comparison studies:
   a. *Method comparison with predicate device*
   Clinical serum samples were obtained from a third party vendor and selected to contain samples below, within and above the medical decision points. One hundred and fifty samples were analyzed in singlicate using the new device and the predicate device. Sample values ranged from 0.2-7.0 ug/ml. Results of the sponsor's analysis based on Passing-Bablok model are shown below:
   Y= 1.043X-0.047, md(95)=0.413, r=0.99

   b. *Matrix comparison:*
   To evaluate the effect of plasma anticoagulants, comparisons of serum samples versus samples containing EDTA, sodium heparin,

and lithium heparin were conducted. Fifteen samples were included for each anticoagulant. No significant bias due to these anticoagulants was observed.

3. Clinical studies:
    a. *Clinical sensitivity:* N/A. (Not typically reviewed for this type of test.)

    b. *Clinical specificity:* N/A. (Not typically reviewed for this type of test.)

4. Clinical cut-off: See expected values.

5. Expected values/Reference range: The therapeutic range for quinidine using this specific assay was not determined. However, therapeutic ranges of serum quinidine are discussed in the literature and cited and discussed in the package insert. Test findings should always be assessed in conjunction with patient's medical history, clinical examination and other medical findings.

M. Conclusion:

I recommend that the Roche Online TDM Quinidine is substantially equivalent to the predicate device.